



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,204	10/19/2000	Janet A. Warrington	3240.1	7262

22886 7590 12/05/2001

AFFYMETRIX, INC
ATTN: CHIEF IP COUNSEL, LEGAL DEPT.
3380 CENTRAL EXPRESSWAY
SANTA CLARA, CA 95051

EXAMINER

JOHANNSEN, DIANA B

ART UNIT	PAPER NUMBER
----------	--------------

1655

DATE MAILED: 12/05/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/693,204

Applicant(s)

WARRINGTON ET AL.

Examiner

Diana B. Johannsen

Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 April 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4. 6) ☐ Other: _____

DETAILED ACTION

Specification

1. The use of the trademark GeneChip® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 are indefinite for failing to recite a final process step that clearly relates back to the claim preamble, and over the recitation of the term "identifying" and the language "indicating a gene...as said maintenance gene" in claim 1. The claims are drawn to a method "for identifying a maintenance gene" yet recite a final process step of

"indicating a gene...as said maintenance gene". The claims do not set forth how "indicating a gene" as a maintenance gene relates to or results in "identifying" that gene. Accordingly, it is unclear as to whether the claims are intended to be drawn to methods for "identifying" a maintenance gene or to methods for "indicating a gene" as a maintenance gene. Further, the language "identifying" is vague and indefinite. Neither the specification nor the prior art provide a clear and limiting definition for this terminology, and it is unclear as to whether, e.g., applicant intends for this language to be equivalent to, e.g., "detecting", whether additional steps would be required to accomplish "identifying", whether the claims would encompass solely mental processes of "identifying", etc. Further, the language "indicating a gene...as said maintenance gene" is vague and indefinite, as it is unclear as to what actual steps might be involved in "indicating". Clarification is required.

Claims 1-8 are indefinite over the recitation of the language "at least one hundred genes in at least two different types of tissues in two different developmental stages". It is unclear as to what is meant by this recitation. For example, it is unclear as to whether applicants' intent is to require the examination of at least two tissues, which tissues must be both of a different type and of a different developmental stage, whether applicants intent is to require at least two tissue types from each of two different developmental stages (i.e., at least 4 tissues), etc. Clarification is required with respect to what tissues are required for the practice of the claimed methods.

Claims 1-8 are indefinite over the recitation of the language "expressed at the same level" in claim 1. The specification discloses that this language does not

necessarily encompass only expression "at the same level" (as the claim recites), but may also encompass expression meeting other criteria (e.g., expression "within ten folds", "within fourfold", expression that is not statistically different, etc.). However, while the specification provides examples of levels of difference that could be considered "the same", the specification does not provide a clear and limiting definition of this language, and there is no fixed meaning for this language in the art. Accordingly, the use of the language "expressed at the same level" in claim 1 renders the metes and bounds of the claims unclear. The claims should be amended so as to provide a clear indication of the expression levels that would meet the requirements of the claimed methods.

Claim 4 is indefinite over the recitation of the language "wherein said determining uses nucleic acid probes". This language does not apprise one of skill in the art as to how said probes would be used to accomplish "determining". Clarification is required.

Claims 5-8 are indefinite because it is unclear as to how or whether the claims are intended to further limit claim 1, from which they depend. Claim 1 requires expression "at the same level". As discussed above, this language renders the claims vague and indefinite, because neither the specification nor the art provided a fixed definition for what would constitute "the same level" of expression. Accordingly, it is unclear as to whether the recitations in claims 5-8, which encompass expression which is not actually "the same", actually further limit claim 1, as is required of proper dependent claims. Clarification is required.

Claims 9-12 are indefinite for failing to recite a final process step that clearly relates back to the claim preamble. The claims are drawn to methods "for comparing

Art Unit: 1655

the expression of a gene in a plurality of biological samples," yet recite a final process step of "evaluating... expression of said gene in said plurality of samples". The claims do not set forth how the step of "evaluating" relates to or results in "comparing". Accordingly, it is unclear as to whether the claims are intended to be drawn to methods of "comparing" or to methods of "evaluating".

Claims 9-12 are indefinite because the list of maintenance genes set forth in claim 9 is not clear and definite. First, applicants have included references to accession numbers from an unidentified database in the claims. As database entries are periodically updated and change over time, their inclusion in the claims renders the claims indefinite. Further, it is unclear as to how the inclusion of accession numbers might be intended to limit the claims (e.g., is applicants intent to require a gene encoded by a particular version of a sequence, to require a molecule from a particular source or having particular characteristics, etc.?). Further, the claims as written include numerous abbreviations and recite many gene names that could refer to more than one type of gene and to genes from more than one type of organism. For example, many types of "porin" are known and porins are found in cells of many different organisms. The claims should be amended so as to provide clear and definite descriptions of the genes encompassed thereby.

Claims 9-12 are indefinite due to the improper expression of alternative limitations in claim 9. "Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a

Markush group, recites members as being 'selected from the group consisting of A, B and C'." (MPEP 2173.05(h)). To overcome this rejection, claim 9 may be amended to recite "and" prior to the last gene recited in the list of genes of claim 9.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 9-12 are rejected under 35 U.S.C. 102(e) as being anticipated by MacLeod et al (U.S. Patent No. 6,221,600 B1 [4/2001; filed 10/8/1999]).

With respect to claim 9 and claims dependent therefrom, it is noted that provisional application 60/161,000 does not disclose all of the genes recited in claim 9. Accordingly, applicant is entitled to an effective filing date of October 19, 2000 with respect to independent claim 9 and claims dependent therefrom.

MacLeod et al disclose methods in which a "set of genes is identified whose expression is relatively constant among different biological samples," which genes are "usually comprised of 'housekeeping' genes" (col 38, lines 35-46). MacLeod et al disclose the use of such sets of genes as "sets of control or standardization genes" in methods of monitoring and quantitating variations in gene expression among different tissue types (see entire reference). MacLeod et al disclose that expression of genes of

Art Unit: 1655

interest are compared with expression of the set of standardization genes (see, e.g., col 38, lines 42-44). It is noted that the "human standardization gene set" disclosed by MacLeod et al comprises at least ten maintenance genes selected from those recited in instant claim 9 (e.g., ribosomal proteins L3, L30, S7, L35, S28, L8, L31, L10, S11, L6). Accordingly, MacLeod et al anticipate the instant claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacLeod et al (U.S. Patent No. 6,221,600 B1 [4/2001; filed 10/8/1999]) in view of Chen et al (U.S. Patent No. 6,245,517 [6/2001; filed 9/28/1999]).

MacLeod et al disclose methods in which a "set of genes is identified whose expression is relatively constant among different biological samples," which genes are "usually comprised of 'housekeeping' genes" (col 38, lines 35-46). MacLeod et al disclose the use of such sets of genes as "sets of control or standardization genes" in methods of monitoring and quantitating variations in gene expression among different tissue types (see entire reference). MacLeod et al disclose that biological samples of his methods may be obtained from different types of tissues at different stages of development (see, e.g., col. 7, lines 7-30). However, as the standardization gene sets taught by MacLeod et al contain fewer than one hundred genes, MacLeod et al do not teach each limitation of the present claims. Like MacLeod et al, Chen et al disclose methods of quantitatively comparing gene expression in different tissues, and disclose the use of sets of housekeeping genes as controls (see entire reference, especially col 18, lines 29-64). Chen et al disclose that for the purposes of his methods, a "carefully selected internal control gene set with about 100 genes provides a robust calibration result," and discloses that results achieved with such a set will be superior to results obtained with "one or two standard genes or an inclusive set of genes". In view of the teachings of Chen et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of identifying standardization genes of MacLeod et al so as to have identified a larger set of standardization genes comprising "at least one hundred genes," as required by the claims. An ordinary artisan would have been motivated to have made such a modification in order to have identified an appropriate set of standardization genes for

use in the methods of Chen et al for the advantage of achieving a "robust calibration result," as suggested by Chen et al. With respect to claim 2, it is noted that an ordinary artisan would have been motivated to have identified as many maintenance/housekeeping genes as possible (including "at least one thousand" such genes) for the advantage of identifying the largest possible pool of genes from which to select a set of approximately one hundred appropriate for use in Chen et al's methods. With respect to claim 4, it is noted that MacLeod et al discloses methods employing nucleic acid probe arrays (col 30, lines 21-34). With respect to claims 5-8, it is noted that MacLeod et al disclose sets of genes whose expression is "relatively constant among different biological samples", which sets meet the requirements of claims 5-8 as written.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:00 am-3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/305-3014 for regular communications and 703/305-4242 for After Final communications.

Application/Control Number: 09/693,204
Art Unit: 1655

Page 10

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B. Johannsen
December 3, 2001.